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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/381,556	01/05/2000	Yuman Fong	MSKP031USNP	4110

21121 7590 08/26/2003

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EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	20

DATE MAILED: 08/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/381,556	FONG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and response received on 6/3/03 has been entered. Claims 1-40 are pending and currently under examination in the instant application. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

Double Patenting

The rejection of claims 1-22, and 38-40 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-40 of U.S. Patent No. 6,051,428 (4/18/00), hereafter referred to as the '428 patent, is maintained. Since the applicants have not traversed the grounds of rejection, the rejection of record stands. However, it is noted that applicants have indicated their willingness to file a terminal disclaimer over US Patent 6,051,428 upon indication that the claims are allowable over the prior art of record.

Claim rejections - 35 U.S.C. 112

The rejection of claims 1-40 are rejected under 35 U.S.C. 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which

applicant regards as the invention, is maintained over claims 4-6 and withdrawn over claims 1-3, and 7-40 in view of applicant's amendments to the claims and/or arguments. However, please note that applicant's arguments have resulted in new grounds of rejection over claims 36-37, see below. Applicant's arguments regarding the rejection of claims 4-6 has been fully considered but has not been found persuasive in overcoming the instant grounds of rejection for reasons of record.

The applicant argues that claim 4 has been amended to recite a step of "administering transduced tumor cells". However, claim 4 has not in fact been amended to recite the indicated limitation. Claims 5-6 depend on claim 4. Therefore, the rejection of record over claims 4-6 stands.

Claims rejections - 35 U.S.C. 101

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 36 and 37 are newly rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The previous office action rejected claims 36 and 37 under 35 U.S.C. 112, second paragraph, for indefiniteness because if the method of claim 1 is actually intended to read only on the production of transduced tumor cells in vivo, without their

being isolated from the mammal, then claim 36 would read on tumor cells present in any mammal including a human. As such, claim 36 would encompass a human, which is not considered patentable subject matter under 35 U.S.C. 101. In response to this rejection, the applicant has stated that the invention is in fact intended to encompass tumor cells present in a human. The applicant argues that since the claims are not specifically directed to a human organism, " [t]he fact that cells may be present in a human does not make the subject matter improper". The office disagrees. If the claimed cells are not isolated from the human subject then the tumor cells, as a product claim, encompass the entire human being. Since the patenting of human beings is not considered statutory, claims which encompass a human being are not statutory subject matter. As such, claim 36 fails to meet the requirements of patentability under 35 U.S.C. 101. This rejection can be overcome by amending the claim to recite "Isolated tumor cells....".

Claims rejections - 35 U.S.C. 102

The rejection of claims 1-3, and 7-40 under 35 U.S.C. 102(e) over U.S. Patent No. 6,344,445, 2/5/02, hereafter referred to as Boursnell et al, is maintained. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant grounds of rejection for reasons of record as discussed in detail below.

The applicant argues that Boursnell does not exemplify tumor cells transduced with HSV amplicons comprising an immunostimulatory molecule and a therapeutic molecule, and

that absent any specific examples, Boursnell et al. does not demonstrate possession or provide an enabling disclosure of such an invention. MPEP 2121.01 states that "'In determining that quantum of prior art disclosure which is necessary to declare an applicant's invention 'not novel' or 'anticipated' within section 102, the stated test is whether a reference contains an 'enabling disclosure'... .'" *In re Hoeksema*, 399 F.2d 269, 158 USPQ 596 (CCPA 1968). A reference contains an "enabling disclosure" if the public was in possession of the claimed invention before the date of invention. "Such possession is effected if one of ordinary skill in the art could have combined the publication's description of the invention with his [or her] own knowledge to make the claimed invention." *In re Donohue*, 766 F.2d 531, 226 USPQ 619 (Fed. Cir. 1985). *In re Donohue* further states, " the fact that an author of a publication did not attempt to make the compound disclosed, without more, will not overcome a rejection based on that publication". Boursnell et al. provides substantial direction for making mixtures of recombinant HSV amplicons and packaged HSV vectors which encode an immunomodulatory or therapeutic gene (Boursnell et al., column 14, lines 17-41, columns 16-23, Figures 1-6, and column 39-40). It is further noted that the claims in the Boursnell Patent in fact recite methods for using these recombinant HSV vectors to transduce cells (Boursnell et al., columns 39-40, claims 1-16). Boursnell et al. further teaches that the HSV vectors may encode more than one genes, preferably one or more cytokines, or combinations of cytokines and costimulatory molecules (Boursnell et al., columns 7-8, and column 14, lines 54-60). Boursnell et al. further teaches that it was well within the skill of the ordinary artisan at the time of filing to make recombinant

vectors, including herpes vectors, that encode more than one immunomodulatory gene, such as an antigen and a cytokine (Boursnell et al., columns 2-3, bridging paragraph). From the detailed description in the Boursnell specification for making a recombinant HSV vector and from the clear indication by Boursnell that methods of making multiply recombinant herpes vectors were known in the art, and in the absence of any evidence to the contrary, the Boursnell et al. patent enables the disclosed mixtures of HSV amplicons and the use of those HSV amplicons and vectors to transduce tumor cells.

In addition, please note that claims 38-40 recite methods of producing an autologous vaccine comprising transducing tumor cells with a herpes simplex virus amplicon containing the gene for an immunostimulatory protein selected from a group consisting of chemokines, intercellular adhesion molecules, and costimulatory factors. These claims do not recite a combination of an immunostimulatory protein and a therapeutic gene. Claims 38-40 are in fact directly anticipated by claims 12-14 of the Boursnell et al. patent.

The applicant further argues that the case law cited in the previous office action regarding patentable weight accorded to intended use is directed to product claims and product by process claims, and not to method claims. The claims at issue are product claims, claims 23-37, and methods of producing a vaccine, claims 1-3, 7-22, and 38-40. The case law previously cited states that a preamble is generally not accorded any patentable weight where it merely recites the purpose of a **process** or the intended use of a structure or composition, and where the body of the claim does not depend on the preamble for completeness but, instead, **the**

process steps or structural limitations are able to stand alone. *In re Hirao* , 535 F.2d 67, 190 USPQ 15 (CCPA 1976); *Kropa v. Robie* , 88 USPQ 478, 481 (CCPA 1951), emphasis added. In a claim drawn to a **process of making**, the intended use must result in a manipulative difference as compared to the prior art. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Contrary to applicant's statements, the cited case law appears to be directly on point and makes specific reference to process of making a composition. Claims 1-3, 7-22, and 38-40 are essentially processes for making "autologous vaccines". From the methods steps disclosed in claims 1-3, 7-22, and 38-40, an "autologous vaccine" is made by transducing tumor cells with an HSV amplicon that contains a gene for an immunostimulatory protein (claims 38-40), or one or more species of HSV amplicons that contains a gene for an immunostimulatory protein and a therapeutic gene (claims 1-3, and 7-22). Boursnell et al. teaches the exact same method steps as the instant method claims. Since the transduced tumor cells taught by Boursnell et al. appear to be the same as those disclosed in the instant invention, patentable weight is not granted to the identification of the cells as "autologous vaccines" by the applicants.

Regarding the specific recitation of combinations of IL-2 and IL-12 or RANTES and IL-2 in the claims, please note that Boursnell et al. clearly discloses HSV amplicons and vectors encoding IL-2, IL-12, B7 and RANTES (Boursnell et al., columns 7-8, and column 40, claim 12). As discussed above and in previous office actions, Boursnell et al. further teaches using combinations of these immunostimulatory molecules, particularly combinations of cytokines,

and cytokines and accessory molecules. As such, a fair reading of Boursnell et al. teaches making mixtures of HSV amplicons comprising genes encoding any combination of the recited immunostimulatory genes, including IL-2 and IL-12, and RANTES and B7-1. Thus, for reasons of record, the rejection of claims 1-3, and 7-40 over Boursnell et al. stands.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Monday- Friday from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER